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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,524	06/27/2000	PETER JOHN BURNE	0769.00140	8239

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EXAMINER
PADMANABHAN, KARTIC

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,524	BURNE ET AL.	
	Examiner	Art Unit	
	Kartic Padmanabhan	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *154-168,170-181,184-198 and 200-214* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *154-168,170-181,184-198 and 200-214* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 154-168, 170-181, 211-212, and 214 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergman (US Pat. 5,501,955) in view of Ehrenkranz (WO 96/27129), and May et al. (US Pat. 5,622,871).

Bergman teaches a method for detecting the presence of autoantibodies in biological fluids, such as serum (col. 3, line 67) by a) providing an antigen specific for autoantibody such as thyroid peroxidase; b) providing a substrate having an immobilized antibody specific for the antigen; c) contacting the antigen with a body fluid sample to allow binding of the complex; d) allowing the mixture to flow into the test tube to contact the immobilized monoclonal antibody; e) providing labeling means such as labeled non-immobilized monoclonal antibody to allow binding to the complex, which is an indication of the presence of autoantibody in a sample of body fluid (fig 1 and cols. 3-4). The reference also teaches various formats for the detection of autoantibodies. The reference states that sandwich complexes with a specification of suitable properties for detection of certain autoantibodies can be tailored when both the immobilized and labeled antibodies are monoclonal (col. 4, lines 50-55). The reference also teaches three different competitive situations involving analyte-antibody analysis. In Fig 1, analyte competes for the same binding site as the immobilized antibody. In Fig 2, analyte competes for the same binding site as the labeled antibody. In Fig 3, analyte competes for the same binding site as both labeled and immobilized antibodies. The reference does not teach the use of first and second immobilized antibodies that bind to distinct binding sites on an antigen or of a test strip as the substrate.

Ehrenkranz teaches a TSH immunoassay, wherein the assay comprises a labeled antibody in mobile phase, and a second antibody in a stationary phase. The antibodies are chosen such that they each bind to different epitopes on TSH, such that both antibodies may bind to TSH to form a sandwich (abstract). The assay may be conducted on whole blood, serum, or plasma (page 3). The assay is conducted in a test strip format.

May et al. teach a test strip format in which assays involving specific binding or immunoassays may be formatted in a test strip to provide convenience for home or clinical use. A sample may be applied to a portion of the test strip and allowed to permeate through the test material. A control zone may be designed to detect unrelated signal to the user that the device is working. The sample progresses to a detection zone where a specific binding partner for the sample analyte is immobilized. Analyte concentration may be determined by a labeled reagent that can be incorporated within the test strip or applied thereto (col. 1, lines 35-60). Direct labels such as metallic sols (e.g. gold) can be used for an analytical result (col. 5, lines 29-32). The substrates involved in the test strip are porous membranes such as nitrocellulose (col. 7, lines 5-10).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergman et al. by providing a multivalent antigen such as TSH and antibodies specific for the pertinent epitopes as taught by Ehrenkranz because this assay method provides for a selective, sensitive, and rapid immunoassay. It would have also been obvious to conduct the method of Bergman in a test strip format as taught by Ehrenkranz and May et al. because the use of a test strip provides for rapid analytical results with a great degree of convenience and little required involvement from the user. In addition, although the references only specifically teach the labeling of antibodies and not antigens to monitor binding of the antigen to autoantibodies, one of skill in the art would have known that the labeling of antigens would have achieved the same end result, and such labeling is deemed to be routine optimization in the art.

5. Claims 184-198 and 200-210 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergman (US Pat. 5,501,955) in view of Ehrenkranz (WO 96/27129) and May et al. (US Pat. 5,622,871) as applied to claims 154-168, 170-181, 211-212, and 214 above, and further in view of Foster et al. (US Pat. 4,444,879).

Bergman, Ehrenkranz, and May et al. teach a modified detection method as discussed above. However, the references do not teach a kit.

Foster et al. teach a kit in which an immunoassay of the invention is incorporated. The kit contains a substrate, buffers, and other reagents, controls, instructions, containers, and any other pertinent components of the immunoassay of the invention (col. 15, lines 12-34).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the modified method of Bergman. Ehrenkranz, and May et al. by incorporating a kit containing all the necessary reagents and supplies, as taught by Foster et al. because kits are well known in the art and are widely recognized for their advantages of economy and convenience.

6. Claim 213 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergman (US Pat. 5,501,955) in view of Ehrenkranz (WO 96/27129) and May et al. (US Pat. 5,622,871) as applied to claims 154-168, 170-181, 211-212, and 214 above, and further in view of Luo et al. (US Pat. 5,229,073).

Bergman, Ehrenkranz, and May et al. teach a modified detection method as discussed above. However, the references do not teach the use of separation means for separating blood cells from plasma.

Luo et al. teach a competitive immunoassay using a test strip. The test strip of the reference can include filtration means above the application pad and between the application pad and porous strip. The filter means may be used to remove red blood cells from a sample of whole blood, such that plasma is the fluid received by the application pad and transferred to the porous strip.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the modified method of Bergman, Ehrenkranz, and May et al. by incorporating separation means for separating blood cells from plasma because filtration means are well known and commonly used in test strips. Depending on the blood fraction one wished to analyze, one would have had a reasonable expectation of success in including separation means in the test strip to exclude unwanted fraction. In addition, Ehrenkranz teaches the TSH may be quantified in whole blood, red blood cells, or plasma.

Response to Arguments

7. Applicant's arguments filed June 12, 2003 have been fully considered but they are not persuasive.

8. In response to applicant's argument that there is no teaching in Bergman as to the use of first and second immobilized antibodies that bind to distinct binding sites on a common antigen, the examiner agrees. However, Ehrenkranz, as a secondary reference, was relied upon for this feature. It is also noted that the claims do not require both antibodies to be immobilized, as applicant has repeated used "and/or," which requires that only one antibody be immobilized.

9. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the

teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would have been motivated to combine the teachings of Bergman to use a test strip, as taught by May et al. due to the recognized ease and convenience of such an assay format. There is no reason to believe that the complex formed in Bergman would not migrate through the test strip and bind to the immobilized antibody in the detection zone, especially when considering that May also assays biological fluids. Simply because such a modification has not been proposed or performed in the past does not render such a modification lacking in motivation or obviousness. Further, when the teachings of May and Ehrenkranz are combined with Bergman, the examiner maintains that the claimed invention is taught.

10. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

11. Applicant's arguments that neither Bergman nor May teach separation means for separating blood cells from plasma are accurate; however, Luo et al. has been relied upon to cure this deficiency.

12. Applicant's arguments regarding claims 14 that Bergman teaches away from labeling antigens are not convincing. Although Bergman clearly prefers the use of labeled antibodies, there is nothing in the reference to suggest that the invention would not work with labeled antigen. The reference simply prefers to use labeled antibody due to the sensitive nature of the antigens of the difficulty in labeling them.

13. Applicant's arguments with respect to the Janeway reference are moot, as the reference has no longer been applied in any of the outstanding rejections. Applicant's arguments regarding the Foster reference are based primarily on the premise that the combination of Bergman. Ehrenkranz, and May is improper, a position which has already been addressed and rejected.

Conclusion

Claims 154-168, 170-181, 184-198, and 200-214 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kartic Padmanabhan whose telephone number is 703-305-0509. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Kartic Padmanabhan
Patent Examiner
Art Unit 1641

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LONG V. LE
SUPERVISORY PATENT EXAMINER
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08/22/03